

CLAIMS

1. A light chain (L chain) variable region (V region) of mouse monoclonal antibody to the human interleukin-6 receptor (IL-6R).

5 2. An L chain V region according to claim 1, having an amino acid sequence shown in any one of SEQ ID NOs: 24, 26, 28 and 30.

3. A heavy chain (H chain) V region of a mouse monoclonal antibody to the human IL-6R.

10 4. An H chain V region according to claim 3, having an amino acid sequence shown in SEQ ID NOs: 25, 27, 29 and 31.

5. A chimeric antibody to the human IL-6R, comprising:

15 (1) an L chain comprising a human L chain constant region (C region) and an L chain V region of a mouse monoclonal antibody to the human IL-6R; and

(2) an H chain comprising a human H chain C region and an H chain V region of a mouse monoclonal antibody to the human IL-6R.

20 6. A chimeric antibody according to claim 5, wherein the mouse L chain V region has an amino acid sequence shown in any one of SEQ ID NOs: 24, 26, 28 and 30; and the mouse H chain V region has an amino acid sequence shown in any one of SEQ ID NOs: 25, 27, 29 and 31.

7. Complementarity determining regions (CDRs) of an L chain V region of a mouse monoclonal antibody to the human IL-6R.

30 8. CDR according to claim 7, having amino acid sequence shown in any one of SEQ ID NOs: 24, 26, 28 and 30 wherein the stretch of the amino acid sequence is defined in Table 9.

35 9. CDR of an H chain V region of a mouse monoclonal antibody to the human IL-6R.

10. CDR according to claim 9, having amino acid sequence shown in any one of SEQ ID NOs: 25, 27, 29, and

0914385-071398
SECRET

31 wherein the stretch of the amino acid sequence is defined in Table 9.

11. A reshaped human L chain V region of an antibody to the human IL-6R, comprising:

- 5 (1) framework regions (FRs) of a human L chain V region, and
(2) CDRs of an L chain V region of a mouse monoclonal antibody to the human IL-6R.

10 12. A reshaped human L chain V region according to claim 11, wherein the CDRs have amino acid sequences shown in any one of SEQ ID Nos.: 24, 26, 28 and 30 wherein the stretches of the amino acid sequences are defined in Table 9.

15 13. A reshaped human L chain V region according to claim 11, wherein the FRs are derived from the human antibody REI.

14. A reshaped human L chain V region according to claim 11, having an amino acid sequence shown as RV_La or RV_Lb in Table 2.

20 15. A reshaped human L chain V region according to claim 11, having an amino acid sequence shown as RV_L in Table 5.

16. A reshaped human H chain V region of an antibody to the human IL-6R, comprising:

- 25 (1) FRs of a human H chain V region, and
(2) CDRs of an H chain V region of a mouse monoclonal antibody to the human IL-6R.

30 17. A reshaped human H chain V region according to claim 16, wherein the CDRs have amino acid sequences shown in SEQ ID NOS: 25, 27, 29 and 31 wherein the stretches of the amino acid sequences are defined in Table 9.

35 18. A reshaped human H chain V region according to claim 16, wherein the FRs are derived from the human antibody NEW or HAX.

19. A reshaped human H chain V region according to

0914285-071396

claim 16, having an amino acid sequence shown in Table 3 as RV_{Ha}, RV_{Hb}, RV_{Hc}, RV_{Hd}, RV_{He} or RV_{Hf}.

20. A reshaped human H chain V region according to claim 17, having an amino acid sequence shown as RV_{Ha}, RV_{Hb}, RV_{Hc} or RV_{Hd} in Table 7.

21. An L chain of a reshaped human antibody to human IL-6R comprising:

- (1) a human L chain C region; and
- (2) an L chain V region comprising human L chain FRs and L chain CDRs of mouse monoclonal antibody to human IL-6R.

22. A reshaped human antibody L chain according to claim 21, wherein the human L chain C region is a human γ -1C region, the human L chain FRs are derived from REI, and the L chain CDRs have amino acid sequences shown in SEQ ID Nos. 24, 26, 28 and 30 wherein the stretches of the amino acid sequences are defined in Table 9.

23. A reshaped human antibody L chain according to claim 21, wherein the L chain V region has an amino acid sequence shown as RV_{La} or RV_{Lb} in Table 2.

24. A reshaped human antibody L chain according to claim 21, wherein the L chain V region has an amino acid sequence shown as RV_L in Table 5.

25. An H chain of a reshaped human antibody to human IL-6R comprising:

- (1) a human H chain C region, and
- (2) an H chain V region comprising human H chain FRs, and H chain CRDs of mouse monoclonal antibody to human IL-6.

26. A reshaped human antibody H chain according to claim 25, wherein the human H chain C region is human kc region, the human H chain FRs are derived from NEW or HAX, the H chain CDRs have amino acid sequences shown in SEQ ID NOS: 25, 27, 29 or 31 wherein the stretches of the amino acid sequences are defined in Table 9.

27. A reshaped human antibody H chain according to

09114285 071398

claim 25, wherein the H chain V region has an amino acid sequence shown as RV_Ha, RV_Hb, RV_Hc or RV_Hd in Table 3.

28. A reshaped human antibody H chain according claim 25, wherein the H chain V region has an amino acid sequence shown as RV_Ha, RV_Hb, RV_Hc or RV_Hd in Table 6, or RV_Ha, RV_Hb, RV_Hc or RV_Hc in Table 7.

29. A reshaped antibody to the human IL-6R, comprising:

(A) an L chain comprising,
(1) a human L chain C region, and
(2) an L chain V region comprising human L chain FRs, and L chain CDRs of a mouse monoclonal antibody to the human IL-6R; and

(B) an H chain comprising,
(1) a human H chain C region, and
(2) an H chain V region comprising human H chain FRs, and H chain CDRs of a mouse monoclonal antibody to the human IL-6R.

30. A reshaped human antibody according to claim 29, wherein the L chain CDRs have amino acid sequences shown in any one of SEQ ID NOs: 24, 26, 28 and 30 wherein the stretches of the amino acid sequences are defined in Table 9; the H chain CDRs have amino acid sequence shown in any one of SEQ ID NOs: 25, 27, 29 and 31 wherein the stretches of the amino acid sequences are defined in Table 9; the human L chain C region and human L chain FRs are derived from the REI; and the human H chain C region and human FRs are derived from the NEW or HAX.

31. A reshaped human antibody according to claim 29, wherein the L chain V region has an amino acid sequence shown as RV_La or RV_Lb in Table 2.

32. A reshaped human antibody according to claim 29, wherein the L chain V region has an amino acid sequence shown as RV_L in Table 5.

33. A reshaped human antibody according to

0914285.071398

claim 29, wherein the H chain V region has an amino acid sequence shown in Table 3 as RV_{Ha}, RV_{Hb}, RV_{Hc}, RV_{Hd}, RV_{He} or RV_{Hf}.

5 34. A reshaped human antibody according to claim 29, wherein the H chain V region has an amino acid sequence shown as RV_{Ha}, RV_{Hb}, RV_{Hc} or RV_{Hd} in Table 6, or RV_{Ha}, RV_{Hb}, RV_{Hd} in Table 7.

35. A DNA coding for an L chain V region of a mouse monoclonal antibody to the human IL-6R.

10 36. A DNA according to claim 35, wherein the L chain V region has an amino acid sequence shown in any one of SEQ ID NOs: 24, 26, 28 and 30.

37. A DNA coding for an H chain V region of a mouse monoclonal antibody to the human IL-6R.

15 38. A DNA according to claim 37, wherein the H chain V region has an amino acid sequence shown in any one of SEQ ID NOs: 25, 27, 29 and 31.

39. A DNA coding for CDR of an L chain V region of a mouse monoclonal antibody to the human IL-6R.

20 40. A DNA coding for CDR according to claim 39, wherein the CDR has an amino acid sequence in any one of SEQ ID NOs: 24, 26, 28 and 30 wherein the stretch of the amino acid sequence is defined in Table 9.

25 41. A DNA coding for CDR of an H chain V region of a mouse monoclonal antibody to the human IL-6R.

42. A DNA coding for CDR according to claim 41, wherein the CDR has an amino acid sequence shown in any one of SEQ ID NOs: 25, 27, 29 and 31 wherein the stretch of the amino acid sequence is defined in Table 9.

30 43. A DNA coding for a reshaped human L chain V region of an antibody to the human IL-6R, wherein the reshaped human L chain V region comprises:

(1) FRs of a human L chain V region, and
(2) CDRs of a mouse L chain V region of a
35 monoclonal antibody to the human IL-6R.

44. A DNA coding for a reshaped human L chain

091425-071598

V region according to claim 43, wherein the CDRs have amino acid sequences shown in any one of SEQ ID NOs: 24, 26, 28 and 30 wherein the stretches of the amino acid sequences are defined in Table 9.

5 45. A DNA coding for a reshaped human L chain V region according to claim 43, wherein the FRs are derived from the REI.

10 46. A DNA according to claim 43, wherein the L chain V region has an amino acid sequence shown as RV_{La} or RV_{Lb} in Table 2.

15 47. A DNA according to claim 43, wherein the L chain V region has an amino acid region shown as RV_L in Table 5.

20 48. A DNA according to claim 43, having a nucleotide sequence shown in SEQ ID No: 57.

25 49. A DNA coding for a reshaped human H chain V region of an antibody to the human IL-6R, wherein the reshaped Human V region comprises:

- 30 (1) FRs of a human H chain V region, and
 (2) CDRs of an H chain V region of a mouse monoclonal antibody to the human IL-6R.

35 50. A DNA coding for a reshaped human H chain V region according to claim 49, wherein the CDRs have amino acid sequences shown in SEQ ID NOs: 25, 27, 29 and 31 wherein the stretches of the amino acid sequences are defined in Table 9.

 51. A DNA coding for a reshaped human H chain V region according to claim 49, wherein the FRs are derived from the NEW or HAX.

 52. A DNA coding for a reshaped human H chain V region according to claim 49, wherein the H chain V region has an amino acid sequence shown as RV_{Ha} , RV_{Hb} , RV_{Hc} , RV_{Hd} , RV_{He} or RV_{Hf} in Table 3.

 53. A DNA according to claim 49, wherein the H chain V region has an amino acid sequence shown as RV_{La} , RV_{Lb} , RV_{Lc} or RV_{Ld} in Table 6, or RV_{Ha} , RV_{Hb} , RV_{Hc} or

09114285-071398

RV_{ED} in Table 7.

54. A DNA according to claim 49, having a nucleotide sequence shown in SEQ ID NO: 56.

55. A DNA coding for a reshaped human L chain of an antibody to the human IL-6R, wherein the reshaped human L chain comprises:

- (1) a human L chain C region; and
- (2) an L chain V region comprising a human FRs, and CDRs of a mouse monoclonal antibody to the human IL-6R.

56. A DNA according to claim 55, wherein the L chain V region has the nucleotide sequence shown in SEQ ID NO: 57.

57. A DNA coding for a reshaped human H chain of an antibody to the human IL-6R, wherein the reshaped human H chain comprises:

- (1) a human H chain C region, and
- (2) a H chain V region comprising human FRs, and CDRs of a mouse monoclonal antibody to the human IL-6R.

58. A DNA according to claim 57, wherein the H chain V region has the nucleotide sequence shown in SEQ ID NO: 56.

59. A vector comprising a DNA according to any one of claims 35, 37, 39, 41, 43, 49, 55 and 57.

60. A host cell transformed or transfected with a vector comprising a DNA according to any one of claims 35, 37, 39, 41, 43, 49, 55 and 57.

61. A DNA coding for a chimeric L chain of an antibody to the human IL-6R, wherein the chimeric L chain comprises:

- (1) a human L chain C region; and
- (2) an L chain V region of a mouse monoclonal antibody to the human IL-6R.

62. A DNA coding for a chimeric H chain of an antibody to the human IL-6R wherein the chimeric H chain

014285-071398
06 OCT 20 09:58:47

comprises:

- (1) a human H chain C region; and
- (2) an H chain V region of a mouse monoclonal antibody to the human IL-6R.

5 63. A process for production of a chimeric antibody to the human IL-6R, comprising the steps of:

10 culturing host cells cotransfected with an expression vector comprising a DNA according to claim 61 and with an expression vector comprising a DNA according to claim 62; and

recovering a desired antibody.

15 64. A process for production of a reshaped human antibody to the human IL-6R, comprising the steps of:

15 culturing host cells cotransfected with an expression vector comprising a DNA according to claim 55 and with an expression vector comprising a DNA according to claim 57; and recovering desired antibody.

20 65. A DNA according to claim 49, having a nucleotide sequence shown in SEQ ID NO: 85, 86 or 94.

20 66. A DNA according to claim 44, having a nucleotide sequence shown in SEQ IN NO: 71.

add 78
AA4

09114285-071398